respectively) had to be reinjected.

(23*R*,24*R*)-4α,23,24-Trimethyl-5α-cholestan-3β-ol (1a): high-resolution MS (70 eV, probe), *m/z* (assignment, relative intensity) 430.4179 ($C_{30}H_{54}O$, M^+, 22), 415.3941 ($C_{29}H_{51}O$, 16), 412.4089 ($C_{30}H_{52}$, 6), 397.3844 ($C_{29}H_{49}$, 15), 341.3194 ($C_{25}H_{41}$, 3), 303.3067 ($C_{22}H_{39}$, 2), 299.2745 ($C_{22}H_{35}$, 2), 290.2988 ($C_{21}H_{38}$, 7), 271.2433 ($C_{20}H_{31}$, 8), 262.2300 ($C_{18}H_{30}$, 8), 247.2056 ($C_{17}H_{27}O$, 38), 229.1957 ($C_{17}H_{25}$, 57), 179.1432 ($C_{12}H_{19}O$, 38), 98.1094 (C_7H_{14}, 100).

(23*S*,24*R*)-23,24-Dimethyl-5α-cholestan-3β-ol (2b): high-resolution MS (70 eV, probe), *m/z* (assignment, relative intensity) 416.4019 ($C_{29}H_{52}O$, M^+, 33), 401.3761 ($C_{28}H_{49}O$, 17), 398.3945 ($C_{29}H_{50}$, 9), 383.3683 ($C_{28}H_{47}$, 13), 359.3289 ($C_{25}H_{43}O$, 4), 344.3456 ($C_{25}H_{44}$, 4), 327.3048 ($C_{24}H_{39}$, 4), 317.2857 ($C_{22}H_{37}O$, 3), 290,2978 ($C_{21}H_{38}$, 6), 285.2584 ($C_{21}H_{33}$, 5), 257.2268 ($C_{19}H_{29}$, 14), 248.2140 ($C_{17}H_{28}O$, 11), 233.1904 ($C_{16}H_{25}O$, 64), 215.1802 ($C_{16}H_{23}$, 74), 165.1275 ($C_{11}H_{17}O$, 42), 98.1091 (C_7H_{14}, 100).

(23*R*,24*R*)-4α,23,24-Trimethyl-5α-cholestan-3-one (6a): high-resolution MS (70 eV, probe), *m/z* (assignment, relative intensity) 428.4029 ($C_{30}H_{52}O$, M^+, 25), 413.3791 ($C_{29}H_{49}O$, 14), 357 (3), 331.2992 ($C_{23}H_{39}O$, 16), 315.2695 ($C_{22}H_{35}O$, 3), 287.2377 ($C_{20}H_{31}O$, 6), 269.2286 ($C_{20}H_{29}$, 2), 260.2134 ($C_{18}H_{28}O$, 13), 245.1901 ($C_{17}H_{25}O_1$, 100), 231.1743 ($C_{16}H_{23}O$, 23), 177.1641 ($C_{13}H_{21}$, 3), 177.1278 ($C_{12}H_{17}O$, 21), 98.1092 (C_7H_{14}, 77).

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Registry No. **1a**, 86708-32-9; **1b**, 86708-33-0; **1c**, 86708-34-1; **1d**, 86708-35-2; **1e**, 77617-71-1; **1f**, 86708-36-3; **1i**, 58670-63-6; **1j**, 81445-03-6; **2a**, 85505-68-6; **2b**, 85505-67-5; **2c**, 86708-37-4; **2d**, 86708-38-5; **2g**, 81520-53-8; **3b**, 86708-39-6; **3g**, 64783-84-2; **3j**, 81445-04-7; **4f**, 86708-40-9; **5a**, 86708-41-0; **5b**, 86708-42-1; **5c**, 86708-43-2; **5d**, 86708-44-3; **6a**, 86708-45-4; **6b**, 86709-22-0; **6c**, 86708-46-5; **6d**, 86708-47-6; **6f**, 86708-48-7; 23(*R*),24(*S*)-dimethyl-5α-cholestan-3β-ol *p*-bromobenzoate, 86668-14-6; fucosterol, 17605-67-3; cholesterol, 57-88-5; 24-methylenecholesterol, 474-63-5.

Studies of Vitamin D Oxidation. 3. Dye-Sensitized Photooxidation of Vitamin D and Chemical Behavior of Vitamin D 6,19-Epidioxides

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Dye-sensitized photooxidation of vitamin D and the chemical reactions of the resulting oxidation products have been studied in detail. Vitamin D undergoes 1,4-cycloaddition and ene-type reactions with singlet oxygen to yield two C(6) epimers of 6,19-epidioxyvitamin D (**3** and **4**) as the major products (55–65% total isolated yields) and two C(6) epimers of the $\Delta^{4,7,10(19)}$ 6-hydroperoxide (**5** and **6**) as the minor products (15–25% total yields). The structures of the oxidation products are determined unambiguously by spectral data in combination with X-ray analysis. The chemical behavior of the endoperoxides **3** and **4** is examined in the reactions with basic reagents, Lewis and proton acids, transition-metal complexes, and reducing agents.

As a part of our studies[1] of the chemistry of the conjugated triene group of vitamin D, which is believed to play an important role in the biological activity of the vitamin,[2] we have been investigating the oxidation of the triene group. The oxidation is of interest not only from the chemical but also from the biological point of view, because vitamin D apparently undergoes biological oxidation at the unsaturated part,[3] as unsaturated fatty acids do in the well-known biosynthesis of prostaglandins and leucotrienes.[4] Seeming to support this possibility is the recent

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(3) Although many vitamin D metabolites were identified, the only one with an altered triene structure was 19-nor-7,8-epoxy-25-hydroxy-10-oxovitamin D_3: DeLuca, H. F.; Schnoes, H. K.; Tanaka, Y. U.S. Patent 4 229 359, 1980.

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Table I. Photooxidation of Vitamin D_3 (1a) and D_2 (1b)

entry	substrate (mg)	solvent (mL)	sensitizer[a] (mg)	time, h	product isolated yield, % 3	4	5	6
1	1a (100)	EtOH (100)	RB (100)	3	26	29	11	7
2	1a (100)	CH_2Cl_2 (100)	RB (100)	0.6	29	22	11	7
3	1a (100)	acetone (100)	RB (100)	1.5	28	28	11	7
4	1a (100)	EtOH-benzene (10:90)	RB (100)	0.6	34	30	12	9
5	1a (1000)	EtOH-benzene (20:180)	RB (200)	1.5	33	31	13	9
6	1a (100)	CH_2Cl_2 (100)	TPP (5)	0.8	19	18	±	±
7	1a (100)	acetone (100)	TPP (5)	3	21	26	±	±
8	1b (100)	EtOH (100)	RB (100)	3	25	28	10	7
9	1b (1000)	EtOH-benzene (20:180)	RB (200)	2	31	34	14	10

[a] The abbreviations used are as follows: RB, Rose Bengal; TPP, tetraphenylporphine.

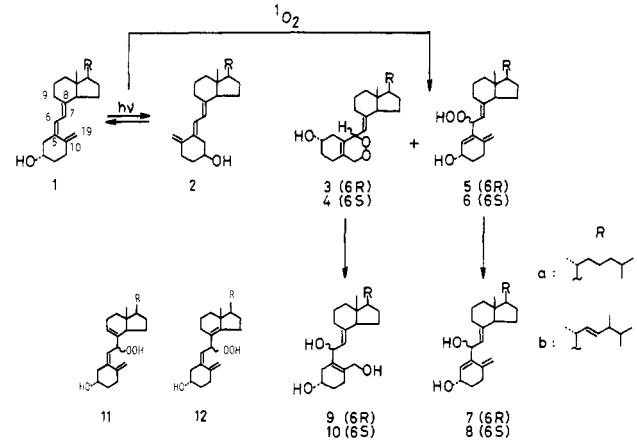
discovery of the receptor protein of the active metabolite of vitamin D,[5] 1,25-dihydroxyvitamin D_3, in human myeloid leukemia cells where lipoxygenase and singlet oxygen are known to be highly active.[6] The oxidation of vitamin D with singlet oxygen is of particular interest because the action of lipoxygenases resembles that of singlet oxygen and also because singlet oxygen is believed to be involved in some cases in peroxidation of lipids in vivo.[7] However, oxidation of vitamin D with singlet oxygen or with other oxidants has received little attention.[8]

Recently we reported the preliminary results of dye-sensitized photooxidation of vitamin D and the successful isolation of the vitamin D–singlet oxygen adducts **3** and **4**.[1a] It has also been found[9] that the vitamin D_3–singlet oxygen adducts **3a** and **4a** are significantly active in intestinal calcium transport and in the elevation of serum calcium and phosphophate levels in vitamin D deficient animals. Now we studied the photooxidation of vitamin D in more detail and found that vitamin D undergoes an ene-type reaction with singlet oxygen in addition to the 1,4-cycloaddition reaction. We have also studied the chemical reactivity of the vitamin D 6,19-epidioxides **3** and **4** and found interesting reactions. Here we report the results in detail.

Results and Discussion

Photooxidation. Photooxidation of vitamin D_3 and D_2 (**1a** and **1b**) was examined in various solvents by using Rose Bengal (RB) and tetraphenylporphine (TPP) as sensitizers. The oxidation was terminated when almost all of the starting vitamin was consumed. The results are summarized in Table I. Vitamin D underwent both 1,4-cycloaddition and ene-type reactions with singlet oxygen at the conjugated triene part. 1,4-Cycloaddition at the *s*-cis diene part was the major oxidation pathway, giving rise to the two isomeric endoperoxides **3** and **4** in 55–65% total isolated yields (Scheme I). When RB was used as the sensitizer, hydroperoxides **5** and **6** were obtained as a result of the ene-type reaction of singlet oxygen. The ene reaction occurred regioselectively at the trisubstituted 5(6) double bond, abstracting the allylic proton at C(4) to yield the two C(6) epimers of the $\Delta^{4,7,10(19)}$ 6-hydroperoxide, **5** and **6**, in 15–25% total yields. These hydroperoxides could not be isolated from the oxidation products by using TPP as the sensitizer, but the formation was detected on TLC among a number of by products with similar polarity. The rate of photooxidation depended on the reaction conditions, especially the kind of solvent used which may affect the lifetime of the singlet oxygen. However, the ratios of the two types of products were little affected by the nature of the solvent. With the same conditions under an atmosphere of oxygen-free inert gas, cis–trans isomerization of the 5(6) double bond occurred in the starting vitamin D, yielding an equilibrium mixture of **1** and the 5,6-trans isomer (**2**), as reported.[10] Since the isomerization is faster than the oxidation, it is clear that the oxidation products are derived from both vitamin D isomers **1** and **2** in a photoequilibrium state.

Scheme I



Characterization of the Photooxidation Products. The structures of the major products **3** and **4** were determined by spectral analysis to be the C(6) epimers of the dioxygen adducts of the starting vitamin D at the s-cis diene part (Table II). The mass spectra and elemental analysis corroborate the molecular composition. The UV spectra show no absorption maximum above 220 nm, indicating the absence of a conjugated double bond. The ^1H NMR spectra exhibit the resonances of the C(19) protons as an AB quartet or a broad singlet at δ 4.0–4.7 and the resonances of the protons at C(6) and C(7) as a pair of doublets at δ 4.7–5.4. The ^{13}C NMR spectra indicate four sp^2 carbons, besides those of the side-chain

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Table II. Spectral Data of Vitamin D Endoperoxides 3 and 4

compd	^{1}H NMR,[a] δ (multiplicity, J in Hz) H-6 and H-7		H-19	^{13}C NMR,[a] δ (multiplicity) C-5 and C-10		C-7	C-8	C-3	C-6	C-19	CD,[b] nm (Δε)
3a	4.88 (d, 10)	5.17 (d, 10)	4.36 (br s)	125.7 (s)	125.7 (s)	115.6 (d)	148.1 (s)	65.9 (d)	76.9 (d)	72.2 (t)	207 (−23.3)
4a	4.76 (d, 9)	5.23 (d, 9)	4.17 (d, 16), 4.60 (d, 16)	126.8 (s)	125.7 (s)	114.5 (d)	149.2 (s)	67.2 (d)	76.8 (d)	72.0 (t)	215 (+6.5)
3b	4.85 (d, 9)	5.12 (d, 9)	4.36 (br s)	125.8 (s)	125.8 (s)	115.5 (d)	148.3 (s)	66.1 (d)	76.9 (d)	72.2 (t)	210 (−17.7)
4b	4.73 (d, 10)	5.18 (d, 10)	4.08 (d, 16), 4.48 (d, 16)	126.7 (s)	125.8 (s)	114.6 (d)	149.3 (s)	67.5 (d)	77.0 (d)	72.1 (t)	211 (+11.3)
3c	4.88 (d, 10)	5.32 (d, 10)	4.30 (d, 15), 4.56 (d, 15)	125.9 (s)	125.4 (s)	114.9 (d)	148.9 (s)	69.0 (d)	76.7 (d)	72.1 (t)	211 (−11.5), 227 (+5.7)
4c	4.78 (d, 10)	5.30 (d, 10)	4.21 (d, 16), 4.63 (d, 16)	126.3 (s)	125.9 (s)	114.3 (d)	149.6 (s)	70.6 (d)	76.8 (d)	72.0 (t)	206 (+7.7), 219 (+5.8)

[a] $CDCl_3$ as the solvent. [b] Hexane as the solvent.

Table III. Spectral Data of Hydroperoxides and Related Compounds

compd	^{1}H NMR,[a] (multiplicity, J in Hz) H_3-18	H-19		H-6 and H-7		H-4	MS, m/e	UV max,[b] nm
5a	0.52 (s)	4.96 (br s)	5.13 (br s)	5.00 (d, 9)	5.54 (d, 9)	6.02 (m)	416, 400, 398, 382	232
6a	0.60 (s)	4.96 (br s)	5.12 (br s)	5.00 (d, 9)	5.53 (d, 9)	6.04 (m)	416, 400, 398, 382	232.5
5b	0.52 (s)	4.97 (br s)	5.0–5.4[c]		5.54 (d, 8)	6.04 (m)	428. 412, 410, 394	235
6b	0.61 (s)	4.95 (br s)	4.9–5.3[c]		5.50 (d, 8)	6.04 (m)	428, 412, 410, 394	234
7a	0.50 (s)	4.94 (br s)	5.06 (br s)	5.10 (d, 8)	5.30 (d, 8)	6.12 (m)	400, 382, 364	234.5
8a	0.60 (s)	4.90 (br s)	5.00 (br s)	5.04 (d, 8)	5.24 (d, 8)	6.05 (m)	400, 382, 364	234.5

[a] $CDCl_3$ as the solvent. [b] 95% EtOH as the solvent. [c] The signals are superimposed by the signals of H-22 and H-23.

carbons in the vitamin D_2 derivatives **3b** and **4b**, and three sp^3 carbons adjacent to an oxygen atom. The stereochemistry of the peroxides **3** and **4** at C(6) was determined by X-ray analysis in collaboration with the CD spectra. Although the pair of epimeric peroxides **3** and **4** show quite similar properties in the spectra described so far, they show contrasting behavior in their CD spectra (Table II). While the epimer **3** shows a negative Cotton effect around 210 nm, due to the homoconjugated double bond, the other isomer, **4**, shows a positive Cotton effect at the same wavelength region. This indicates that the configuration at C(6) has a pronounced effect on the sign of the Cotton effect and that the latter is related to the chirality of these homoconjugated systems. The stereochemistry of crystalline benzoate **3c** of vitamin D_2 endoperoxide **3b** was determined by single-crystal X-ray analysis.[1c,11] The ORTEP drawing of the structure of **3c** (Figure 1) shows that **3c** has the 6*R* configuration. Thus, it was established that around 210 nm the isomers **3b** and **3c** which show a negative Cotton effect have the 6*R* configuration and that the other isomers **4b** and **4c** which show a positive Cotton effect have the 6*S* configuration. The stereochemistry of the vitamin D_3 endoperoxides **3a** and **4a** at C(6) was deduced by comparing their CD spectra with those of the vitamin D_2 derivatives **3b** and **4b**.

The minor products **5** and **6** were determined by spectral analysis and specific chemical reactions to have the

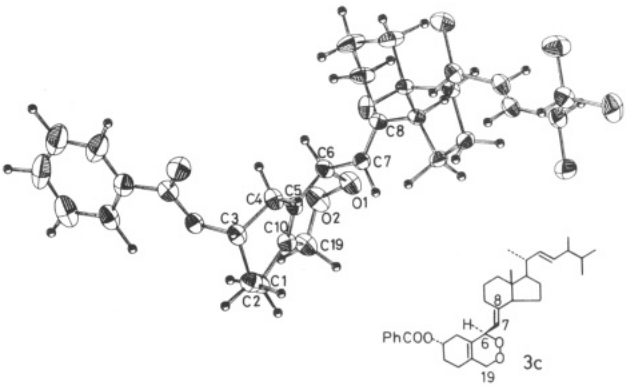

Figure 1. ORTEP drawing of **3c**.

structures of the C(6) epimers of the $\Delta^{4,7,10(19)}$ 6-hydroperoxide (Table III). The mass spectra show a weak molecular ion, indicating the incorporation of two oxygen atoms in the molecule. The fragment ions characteristic for hydroperoxides[12] appear at $M^+ - O$, $M^+ - H_2O$, and $M^+ - H_2O_2$. By Woodward's rule,[13] the absorption maximum in the UV spectra is in good agreement with that calculated for the chromophore of the assigned structures. The ^{1}H NMR spectra exhibit the resonance of the 18-methyl group in the normal region, indicating the absence of an 8(9) or 8(14) double bond.[14] This excludes the alternative structures **11** and **12**. The ^{1}H NMR spectra also exhibit

(11) The crystals were monoclinic $P2_1$ with cell dimensions of a = 16.753 Å, b = 7.446 Å, c = 13.572 Å, and β = 111.4°. Intesities were measured on a Philips PW1100 four-circle diffractometer by using Cu Kα radiation monochromated by a graphite plate, and 3144 independent data were used for the analysis. The structure was elucidated by the direct method with the program MULTAN (Germain, G.; Main, P.; Woolfson, M. M. *Acta Crystallogr. Sect. A* **1971**, *A27*, 368). Positional and thermal parameters were refined by the least-squares method to an R value of 0.092.

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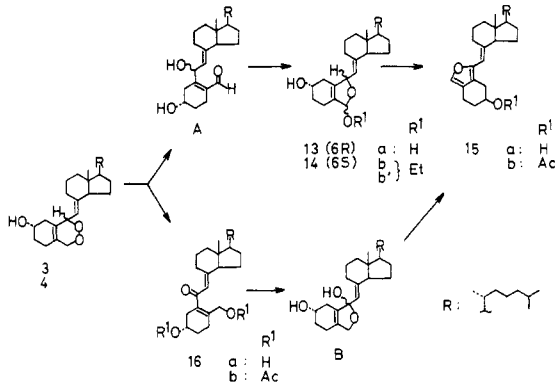
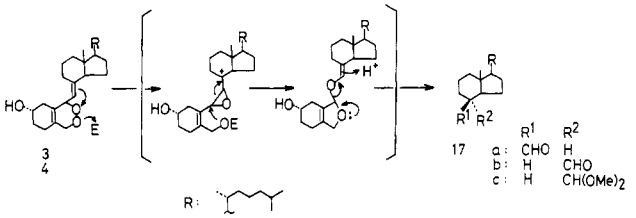
(14) The chemical shifts for the 18-methyl group are indicative of the position of the double bond at the C-ring; the resonances are at δ ca. 0.55, 0.70, and 0.90 for the Δ^7, $\Delta^{8(9)}$, and $\Delta^{8(14)}$ compounds, respectively.

Scheme II



Scheme III



the resonances of the intact exocyclic methylene group at C(19) as a pair of broad singlets, the resonances of the protons at C(6) and C(7) as a pair of doublets, the resonance of a proton at C(4) in an olefinic proton region, and the resonance of H(3) which is shifted to lower field, indicating the presence of the 4(5) double bond. Reduction of the hydroperoxides **5a** and **6a** with triphenylphosphine yielded the diols **7a** and **8a**, the structure of which was verified by the spectral data (Table III). The stereochemistry of the hydroperoxides **5** and **6** and the diols **7** and **8** at C(6) was assigned by comparing their ^{1}H NMR spectra with those of the structurally closely related (6*R*)- and (6*S*)-triols **9** and **10** obtained from (6*R*)- and (6*S*)-vitamin D_3 endoperoxides **3a** and **4a** by reduction with $LiAlH_4$ (see below). In these 6-hydroxy and 6-hydroperoxy derivatives the chemical shift of the 18-methyl group reflects the stereochemistry at C(6); the resonances of 6*R* isomers appear at a field higher than that of the 6*S* isomers by about 0.1 ppm.

Reactions of Vitamin D Endoperoxides. The endoperoxides **3** and **4** are thermally rather stable and are recovered unchanged even after refluxing in xylene for several hours, if the substrate and the solvent used are purified rigorously. However, they are sensitive to bases, acids, and transition-metal complexes.

Reaction with Basic Reagents. On treatment with 5% KOH in methanol at room temperature **3a** was converted within 30 min to furan **15a** (18%) and hemiacetal **13a** (69%, as a mixture of the C(19) epimers) (Scheme II). The structure of **15a** was based on the spectral data. The mass spectrum showed a molecular ion at *m/e* 398. The UV spectrum showed characteristic absorption maxima due to the vinyl furan chromophore at 273 nm (log ϵ 4.20), 283 (4.26), 295.5 (4.12). The ^{1}H NMR spectrum exhibited an aromatic proton on the furan ring at δ 7.15 as a singlet and a vinyl proton at C(7) at δ 5.64 as a singlet. The structure of the hemiacetal **13a** was determined on the basis of the spectral data [mass spectrum, *m/e* 416 (M^+); ^{1}H NMR (acetone-d_6) δ 0.61 (3 H, s, H-18), 3.56–5.90 (6 H, complex signal); IR ($CHCl_3$) 3610, 3420, 2940 cm^{-1}] and the following characteristics: (i) compound **13a** was labile and dehydrated to give the furan **15a** even on standing at room temperature in $CDCl_3$, probably due to the action of a trace of acid in the $CDCl_3$; (ii) on standing in ethanol **13a** was transformed into two isomeric acetals, less polar **13b** and more polar **13b′**, both of which in turn were converted quantitatively to the furan (**15a**) by refluxing in xylene; (iii) the spectral properties of the acetals **13b** and **13b′** were in good agreement with the assigned structure. The mass spectra of **13b** and **13b′** showed a molecular ion at *m/e* 444. The ^{1}H NMR spectra of **13b** and **13b′** showed the resonances of the ethoxy group [**13b**: δ 1.11 (3 H, t, J = 7 Hz), 3.46 (2 H, m). **13b′**: δ 1.12 (3 H, t, J = 7 Hz), 3.51 (2 H, m)], the resonances of the protons at C(6) and C(7) as a pair of doublets [**13b**: δ 4.60 (1 H, d, J = 9 Hz), 5.36 (1 H, d, J = 9 Hz). **13b′**: δ 4.76 (1 H, d, J = 9 Hz), 5.17 (1 H, d, J = 9 Hz)], and the resonance of the acetal proton at C(19) as a singlet (**13b**, δ 5.48; **13b′** δ 5.39). In this reaction, formation of the regioisomer of the hemiacetal **13a**, hemiketal B, was not observed. The hemiketal B formed first probably was dehydrated to the furan **15a** under the reaction conditions, since the hemiacetal **13a** did not afford the furan **15a** under the same reaction conditions. Keto–alcohol **16a**, a precursor of the hemiketal **B**, was trapped as acetate **16b** when **3a** was treated with acetic anhydride–pyridine (1:1, 50 °C); **3a** yielded **15b** (70%) and the ketone **16b** (18%).[15] The transformation of the endoperoxide **3a** to the furan **15a** and the hemiacetal **13a** was also effected by the other basic reagents such as triethylamine (benzene, 80 °C), and CsF (DMF). The two C(6) epimers **3a** and **4a** showed little difference in their chemical behavior in the reactions examined in the present studies. So only the reactions of the 6*R* isomer **3a** will be discussed here as representative of both; the reactions of the 6*S* isomer are described in the Experimental Section.

Reaction with Acidic Reagents. The reactions of the vitamin D endoperoxides **3** and **4** with acidic reagents, in which cleavage of the bond between C(6) and C(7) occurs, are rather unusual. Treatment of **3a** with Lewis acids such as BF_3–Et_2O (benzene, room temperature) and $ZnCl_2$ (xylene, 100 °C) produced aldehyde **17a** in good yields (~85%). The structue of **17a** was deduced on the basis of the spectral data and some chemical reactions. The mass spectrum exhibited a molecular ion at *m/e* 278. The ^{1}H NMR spectrum exhibited an aldehyde proton at δ 9.99 as a singlet. The IR spectrum showed an absorption of the carbonyl group at 1710 cm^{-1}. The β configuration of the formyl group was revealed by the fact that **17a** was converted quantitatively to the thermodynamically more stable isomer **17b** [^{1}H NMR ($CDCl_3$) δ 9.53 (1 H, d, J = 3 Hz, CHO); IR ($CHCl_3$) 1720 cm^{-1}] under equilibrium conditions (EtONa, EtOH). Proton acids effected a similar transformation. Thus, by treatment with HCl (MeOH, 0 °C), **3a** afforded acetal **17c** (38%). The structure of **17c** was based on the spectral data [mass spectrum, *m/e* 324 (M^+); ^{1}H NMR ($CDCl_3$) δ 3.38 (3 H, s, MeO), 3.40 (3 H, s, MeO), 4.06 (1 H, d, J = 4 Hz, acetal CH)] and on the fact that **17c** was transformed quantitatively into the aldehyde **17b** by treatment with acidic aqueous acetone. The configuration of the acetal group was considered to be α (equatrial), since it was produced under thermodynamic conditions. The mechanism shown in Scheme III is suggested for the reactions in acidic conditions.[16] The ste-

(15) The acetyl derivative of the hydroxy aldehyde A was not detected in the reaction of **3a** (or **4a**) with acetic anhydride–pyridine. The hydroxy aldehyde A probably underwent cyclization between the hydroxyl group at C(6) and the 19-formyl group and subsequent dehydration to yield the furan **15**, before it was acetylated at the sterically hindered 6-hydroxyl group.

(16) Products arising from the A-ring part could not be isolated from the reaction.

reoselective formation of the thermodynamically less stable β-formyl derivative **17a** in the Lewis acid catalyzed reactions can be rationalized by assuming a kinetic protonation from the less hindered α side of the molecule.

Reactions with Transition-Metal Complexes. The reactions of endoperoxides catalyzed by transition-metal complexes have been investigated recently in connection with biological transformations.[17] The catalytic reaction of vitamin D endoperoxides **3a** and **4a** was examined by using two types of transition-metal complexes: a Co(II) complex which is capable of inducing the reaction via a one-electron redox process, and a Pd(0) complex which can act as a two-electron transfer reagent. Cobalt–tetraphenylporphine (CoTPP) complex has been known to isomerize sterically compressed bicyclic endoperoxides to diepoxides.[17a] In the particular endoperoxide **3a** this reagent was highly effective in transforming the peroxide exclusively to the hemiacetal **13a** (CH_2Cl_2, −20 to −10 °C; 75% yield). The high regioselectivity observed in this reaction is probably due to the selective formation of a metal complex at the less hindered oxygen atom bound to C(19). Pd(0) complex[17b,c] caused a similar transformation; on treatment with $Pd(Ph_3P)_4$ (benzene, reflux), **3a** afforded **13a** (16%) and **15a** (47%). These reactions probably proceed via the hydroxy enal (A) or the hydroxy enone **16a** as an intermediate, as in the reaction with basic reagents (Scheme II).

Reductions. The endoperoxides **3** and **4** were stable for mild reducing agents such as thiourea,[18] $NaBH_4$, and diimide[19] and for catalytic hydrogenation. The peroxide **3a** was readily reduced by $LiAlH_4$ (Et_2O, room temperature) to triol **9** in good yield (70%). The triol **9** was labile and decomposed even with chromatography on a silica gel column. Purification of the triol **9** was achieved only by using gel chromatography (Sephadex LH-20).

Experimental Section

General Methods. Melting points were determined on a Yanaco micro melting point apparatus and are uncorrected. Infrared (IR) spectra were obtained on a Hitachi 215 spectrophotometer. Proton magnetic resonance (^1H NMR) spectra were recorded with a Varian XL-100 spectrometer with tetramethylsilane as an internal standard. Carbon magnetic resonance (^{13}C NMR) spectra were recorded with a Varian XL-100 spectrometer at 25.16 MHz with tetramethylsilane as an internal reference. Mass spectra (MS) were recorded with a JEOL JMS-D300 GS/MS instrument with an interfaced computer. Ultraviolet (UV) spectra were recorded with a Union Giken SM-401 spectrophotometer. Circular dichroism (CD) spectra were recorded with a JASCO J-20A spectropolarimeter.

Photooxidation of Vitamin D Derivatives (1a and 1b). A solution of vitamin D (**1**) and a sensitizer was placed in an immersion vessel, purged with oxygen, and irradiated with a water-cooled 200-W halogen lamp (Ushio JCV 100-200GS). Oxygen was kept bubbling through the solution during the irradiation and the outside of the vessel was cooled with an ice. The reaction was monitored by TLC and was terminated when almost all of the starting material was consumed. The solvent was evaporated, and the residue was dissolved in ethyl acetate, washed with brine, dried over Na_2SO_4, and evaporated. The residue was chromatographed on silica gel with ethyl acetate–benzene (4:96) as the eluent to afford (6*S*)-epidioxide **4**, (6*R*)-epidioxide **3**, and a mixture of the two epimeric hydroperoxides **5** and **6**, in this order. The two isomeric hydroperoxides **5** and **6** were separated by using HPLC (Lichrosorb Si-60, 0.4 × 25 cm, *i*-PrOH–hexane 7:93) to give less polar **6** and more polar **5**. The results are summarized in Table I. **3a**: high-resolution MS, $C_{27}H_{44}O_3$ requires *m/e* 416.3290, found *m/e* 416.3306; MS, *m/e* 416 (M^+), 398, 285; ^1H NMR ($CDCl_3$) δ 0.56 (3 H, s, H-18), 4.07 (1 H, m, H-3). **4a**: high-resolution MS, $C_{27}H_{44}O_3$ requires *m/e* 416.3290, found *m/e* 416.3270; MS, *m/e* 416 (M^+), 398, 285; ^1H NMR ($CDCl_3$) δ 0.57 (3 H, s, H-18), 3.93 (1 H, m, H-3). **5a**: high-resolution MS, $C_{27}H_{44}O_3$ requires *m/e* 416.3290, found *m/e* 416.3276; ^1H NMR ($CDCl_3$) δ 4.42 (1 H, m, H-3), 7.86 (1 H, s, OOH, D_2O exchangeable); IR ($CHCl_3$) 3350, 2950 cm^{-1}. **6a**: high-resolution MS, $C_{27}H_{44}O_3$ requires *m/e* 416.3290, found *m/e* 416.3280; ^1H NMR ($CDCl_3$) δ 4.43 (1 H, m, H-3), 8.08 (1 H, s, OOH, D_2O exchangeable); IR ($CHCl_3$) 3350, 2950 cm^{-1}. **3b**: high-resolution MS, $C_{28}H_{44}O_3$ requires *m/e* 428.3290, found *m/e* 428.3289; MS, *m/e* 428 (M^+), 410, 285; ^1H NMR ($CDCl_3$) δ 0.55 (3 H, s, H-18), 4.07 (1 H, m, H-3), 5.12 (2 H, m, H-22 and H-23). **4b**: high-resolution MS, $C_{28}H_{44}O_3$ requires *m/e* 428.3290, found *m/e* 428.3295; MS, *m/e* 428 (M^+), 410, 285; ^1H NMR ($CDCl_3$) δ 0.54 (3 H, s, H-18), 3.78 (1 H, m, H-3), 5.12 (2 H, m, H-22 and H-23). **5b**: high-resolution MS, $C_{28}H_{44}O_3$ requires *m/e* 428.3290, found *m/e* 428.3287; ^1H NMR ($CDCl_3$) δ 4.43 (1 H, m, H-3), 7.96 (1 H, s, OOH, D_2O exchangeable); IR ($CHCl_3$) 3350, 2950 cm^{-1}. **6b**: high-resolution MS, $C_{28}H_{44}O_3$ requires *m/e* 428.3290, found *m/e* 428.3289; ^1H NMR ($CDCl_3$) δ 4.42 (1 H, m, H-3), 8.28 (1 H, s, OOH, D_2O exchangeable); IR ($CHCl_3$) 3350, 2950 cm^{-1}.

(6*R*)-6,19-Epidioxy-9,10-secoergosta-5(10),7,22-trien-3β-yl Benzoate (3c). Benzoyl chloride (36 μL, 0.31 mmol) was added to a solution of **3b** (110 mg, 0.26 mmol) in pyridine (0.2 mL) at 0 °C. After 30 min, ice chips were added, and the mixture was extracted with ethyl acetate. The extract was washed with aqueous $NaHCO_3$ and water, dried over Na_2SO_4, and evaporated. The residue was chromatographed on silica gel (6 g) with ethyl acetate–hexane (2:98) as the eluent to yield **3c**: 115 mg (84%); mp 132–133 °C (from hexane); MS, *m/e* 532 (M^+), 514, 392, 267; ^1H NMR ($CDCl_3$) δ 0.59 (3 H, s, H-18), 0.82, 0.84, 0.92, and 1.02 (each 3 H, d, *J* = 7 Hz, H-21, H-26, H-27, and H-28), 4.3 (1 H, d, *J* = 15 Hz, H-19), 4.56 (1 H, d, *J* = 15 Hz, H-19), 4.88 (1 H, d, *J* = 10 Hz, H-6 or H-7), 5.18 (2 H, m, H-22 and H-23), 5.32 (1 H, d, *J* = 10 Hz, H-7, or H-6), 5.4 (1 H, m, H-3), 7.3–7.6 (3 H, m, H–Ar), 8.01 (2 H, dd, *J* = 8, 2 Hz, H–Ar); IR (KBr) 2960, 1710, 1275, 710 cm^{-1}; UV max (95% EtOH) 227 nm (log ε 4.19); $[\alpha]^{30}_D$ +77.5° (*c* 0.69, $CHCl_3$). Anal. Calcd for $C_{35}H_{48}O_4$: C, 78.91; H, 9.08. Found: C, 78.62; H, 9.01.

(6*S*)-6,19-Epidioxy-9,10-secoergosta-5(10),7,22-trien-3β-yl Benzoate (4c). In a similar manner, **4b** (100 mg, 0.23 mmol) was converted to the benzoate **4c**: 98 mg (79%) mp 126–127 °C (from hexane); MS, *m/e* 532 (M^+), 514, 392, 267; ^1H NMR ($CDCl_3$) δ 0.59 (3 H, s, H-18), 0.83, 0.84, 0.92, and 1.03 (each 3 H, d, *J* = 7 Hz, H-21, H-26, H-27, and H-28), 4.21 (1 H, d, *J* = 16 Hz, H-19), 4.63 (1 H, d, *J* = 16 Hz, H-19), 4.78 (1 H, d, *J* = 10 Hz, H-6 and H-7), 5.18 (2 H, m, H-22 and H-23), 5.25 (1 H, m, H-3), 5.30 (1 H, d, *J* = 10 Hz, H-7 or H-6), 7.3–7.6 (3 H, m, H–Ar), 8.01 (2 H, dd, *J* = 8, 2 Hz, H–Ar); IR (KBr) 2960, 1720, 1275, 710 cm^{-1}; UV max (95% EtOH) 229 nm (log ε 4.18); $[\alpha]^{30}_D$ −6.1° (*c* 0.54, $CHCl_3$). Anal. Calcd for $C_{35}H_{48}O_4$: C, 78.91; H, 9.08. Found: C, 79.06; H, 9.13.

(6*R*)-9,10-Secocholesta-4,7,10(19)-triene-3β,6-diol (7a). A solution of **5a** (10 mg, 2.4×10^{-2} mmol) and triphenylphosphine (6.5 mg, 2.5×10^{-2} mmol) in benzene (600 μL) was stirred at room temperature for 20 min. The solvent was evaporated, and the residue was chromatographed on silica gel (3 g) with ethyl acetate–hexane (1:1) as the eluent to afford diol **7a**: 8.3 mg (86%); high-resolution MS, $C_{27}H_{44}O_2$ requires *m/e* 400.3341, found *m/e* 400.3339; ^1H NMR ($CDCl_3$) δ 4.40 (1 H, m, H-3); IR ($CHCl_3$) 3610, 3400, 2950 cm^{-1}.

(6*S*)-9,10-Secocholesta-4,7,10(19)-triene-3β,6-diol (8a). In a similar manner, **6a** (8 mg, 1.9×10^{-2} mmol) was treated with triphenyl phosphine (5.2 mg, 2×10^{-2} mmol) to afford **8a**: 6 mg (78%); high-resolution MS, $C_{27}H_{44}O_2$ requires *m/e* 400.3341, found *m/e* 400.3324; ^1H NMR ($CDCl_3$) δ 4.38 (1 H, m, H-3); IR ($CHCl_3$) 3600, 3410, 2950 cm^{-1}.

Reaction of Endoperoxides 3a and 4a with Methanolic KOH. Peroxide **3a** (55 mg, 1.3×10^{-1} mmol) was dissolved in 5% methanolic KOH (3 mL), and the solution was stored at room

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temperature for 30 min. The mixture was diluted with CH_2Cl_2, washed with brine, dried over Na_2SO_4, and evaporated. Chromatography of the residue on silica gel (5 g) with ethyl acetate–hexane (2:8) as the eluent gave furan **15a** (9.5 mg, 18%). Further elution with ethyl acetate–hexane (8:2) afforded hemiacetal **13a**: 38 mg (69%); MS, *m/e* 416 (M^+), 398, 285, 191, 190, 151; ^1H NMR (acetone-d_6) δ 0.61 (3 H, s, H-18) 3.56–5.90 (6 H, complex); IR ($CHCl_3$) 3610, 3420, 2940 cm^{-1}. For **15a**: MS, *m/e* 398 (M^+), 285, 191, 190, 151; ^1H NMR (acetone-d_6) δ 0.62 (3 H, s, *H*-18), 3.99 (1 H, m, H-3), 5.64 (1 H, s, H-7), 7.15 (1 H, s, H-19); IR ($CHCl_3$) 2940 cm^{-1}; UV max (95% EtOH) 273.5 nm (log ϵ 4.20), 283 (4.26), 295.5 (4.12).

In a similar manner, **4a** (100 mg, 2.4×10^{-1} mmol) was transformed into **15a** (18 mg, 19%) and **14a** (71 mg, 71%) on treatment with 5% methanolic KOH (5 mL). **14a**: MS, *m/e* 416 (M^+), 398, 285, 191, 190, 151; ^1H NMR (acetone-d_6) δ 0.60 (3 H, s, H-18), 3.50–5.93 (6 H, complex).

Hemiacetal **13a** (30 mg) was dissolved in 5% methanolic KOH (2 mL), and the solution was stored at room temperature for 30 min. After a similar workup and chromatographic purification, 27 mg (90%) of **13a** was recovered unchanged.

(6*R*)-6,19-Epoxy-19-ethoxy-9,10-secocholesta-5(10),7-dien-3β-ols (13b and 13b'). Hemiacetal **13a** (40 mg, 9.6×10^{-2} mmol) was dissolved in EtOH, and the solution was stored at 3 °C for 3 days and then at room temperature for 4 days. After evaporation of the solvent, the residue was purified by using HPLC (μ-Porasil, 0.79 × 30 cm, 5:95 *i*-PrOH-hexane) to afford less polar **13b** (22 mg, 52%) and more polar **13b'** (15 mg, 35%). **13b**: MS, *m/e* 444 (M^+), 398, 285, 151; ^1H NMR (acetone-d_6) δ 0.60 (3 H, s, H-18), 1.11 (3 H, t, J = 7 Hz, EtO), 3.46 (2 H, m, EtO), 3.68 (1 H, d, J = 4.5 Hz, OH), 3.88 (1 H, m, H-3), 4.60 (1 H, d, J = 9 Hz, H-6 or H-7), 5.36 (1 H, d, J = 9 Hz, H-7 or H-6), 5.48 (1 H, s, H-19); IR ($CHCl_3$) 3400, 2955 cm^{-1}. **13b'**: MS, *m/e* 444 (M^+), 398, 285, 151; ^1H NMR (acetone-d_6) δ 0.60 (3 H, s, H-18), 1.12 (3 H, t, J = 7 Hz, EtO), 3.51 (2 H, m, EtO), 3.70 (1 H, d, J = 4.5 Hz, OH), 3.90 (1 H, m, H-3), 4.76 (1 H, d, J = 9 Hz, H-6 or H-7), 5.17 (1 H, d, J = 9 Hz, H-7 or H-6), 5.39 (1 H, s, H-19); IR ($CHCl_3$) 3400, 2955 cm^{-1}.

(6*S*)-6,19-Epoxy-19-ethoxy-9,10-secocholesta-5(10),7-dien-3β-ols (14b and 14b'). In a similar manner, hemiacetal **14a** (40 mg) was converted to acetals **14b** (15 mg, 35%) and **14b'** (22 mg, 52%) on standing in ethanol. **14b**: MS, *m/e* 444 (M^+), 398, 285, 151; ^1H NMR ($CDCl_3$) δ 0.60 (3 H, s, H-18), 1.25 (3 H, t, J = 7 Hz, EtO), 3.66 (2 H, m, EtO), 4.03 (1 H, m, H-3), 4.92 (1 H, d, J = 8 Hz, H-6 or H-7), 5.33 (1 H, d, J = 8 Hz, H-7 or H-6), 5.60 (1 H, s, H-19); IR ($CHCl_3$) 3440, 2950 cm^{-1}. **14b'**: MS, *m/e* 444 (M^+), 398, 285, 151; ^1H NMR ($CDCl_3$) δ 0.60 (3 H, s, H-18), 1.24 (3 H, t, J = 7 Hz, EtO), 3.68 (2 H, m, EtO), 4.10 (1 H, m, H-3), 4.74 (1 H, d, J = 8 Hz, H-6 or H-7), 5.59 (1 H, d, J = 8 Hz, H-7 or H-6), 5.66 (1 H, s, H-19); IR ($CHCl_3$) 3450, 2950 cm^{-1}.

6,19-Epoxy-9,10-secocholesta-5,7,10(19)-trien-3β-ol (15a). (A) From Hemiacetal 13a. A solution of **13a** (34 mg, 8.2×10^{-2} mmol) in $CDCl_3$ (500 μL) was kept at room temperature for 2 h. The solvent was evaporated, and the residue was chromatographed on silica gel (5 g) with ethyl acetate–hexane (1:1) as the eluent to yield furan **15a** (31 mg, 95%).

(B) From Acetals 13b and 13b'. A solution of acetal **13b** (2 mg) in xylene (1 mL) was refluxed for 1 h. The solvent was evaporated, and the residue was purified on TLC (silica gel; ethyl acetate–hexane, 15:75) to give **15a** (1.8 mg, 94%).

In a similar manner, **13b'** (3 mg) was converted to **15a** (2.5 mg, quantitative).

Reaction of Endoperoxides 3a and 4a with Acetic Anhydride–Pyridine. Acetic anhydride (2 mL) was added to a solution of **3a** (95 mg) in pyridine (2 mL), and the mixture was stirred at 80 °C for 3 h. The mixture was evaporated to dryness in vacuo. The residue was dissolved in ethyl acetate, and the solution was washed with brine, dried over Na_2SO_4, and evaporated. Chromatography of the residue on silica gel (5 g) with ethyl acetate–hexane (8:92) as the eluent gave **15b** (63 mg, 63%). Further elution with ethyl acetate–hexane (15:85) afforded **16b** (20 mg, 18%). **15b**: MS, *m/e* 440 (M^+), 380; ^1H NMR (acetone-d_6) δ 0.62 (3 H, s, H-18), 1.97 (3 H, s, Ac), 5.05 (1 H, m, H-3), 5.58 (1 H, s, H-7), 7.13 (1 H, s, H-19); IR ($CHCl_3$) 2950, 1720 cm^{-1}; UV max (95% EtOH) 237.5 nm (log ϵ 4.22), 283 (4.29), 295.5 (4.17). **16b**. MS, *m/e* 500 (M^+), 440, 380, 267; ^1H NMR ($CDCl_3$) δ 0.59 (3 H, s, H-18), 2.08 (6 H, s, Ac), 4.71 (2 H, s, H-19), 5.08 (1 H, m, H-3), 5.92 (1 H, s, H-7); IR ($CHCl_3$) 2960, 1725, 1590 cm^{-1}; UV max (95% EtOH) 262 nm (log ϵ 4.08).

In a similar manner, **4a** (112 mg) was treated with acetic anhydride–pyridine to afford **15b** (83 mg, 70%) and **16b** (24 mg, 18%).

Reaction of Endoperoxides 3a and 4a with Triethylamine. A solution of **3a** (50 mg) and triethylamine (50 μL) in benzene (2 mL) was heated at 80 °C for 4.5 h. The mixture was evaporated to dryness, and the residue was chromatographed on silica gel (5 g) to give furan **15a** (25 mg, 52%) and hemiacetal **13a** (13 mg, 26%).

In a similar manner, **4a** (50 mg) was treated with triethylamine to yield **15a** (23 mg, 48%) and **14a** (10 mg, 20%).

Reaction of Endoperoxides 3a and 4a with CsF. To a solution of **3a** (45 mg, 0.11 mmol) in DMF (2 mL) was added CsF (16 mg, 0.11 mmol), and the mixture was stirred for 2 h at room temperature. The mixture was diluted with ethyl acetate, washed with water, dried over Na_2SO_4, and evaporated. The residue was chromatographed on silica gel (5 g) to give **15a** (16 mg, 37%) and **13a** (12 mg, 27%).

In a similar manner, **4a** (30 mg) was converted to **15a** (11 mg, 38%) and **14a** (7 mg, 23%) on treatment with CsF in DMF.

Reaction of Endoperoxides 3a and 4a with Boron Trifluoride Etherate. To a solution of **3a** (50 mg, 1.2×10^{-1} mmol) in benzene (2 mL) was added BF_3–etherate (16 μL, 1.3×10^{-1} mmol) at 0 °C. The reaction mixture turned to dark brown. After 25 min, ice chips were added, and the mixture was extracted with chloroform. The extract was washed with brine, dried over Na_2SO_4, and evaporated. The residue was chromatographed on silica gel (4 g) with benzene–hexane (1:3) as the eluent to give **17a**: 28 mg (84%); MS, *m/e* 278 (M^+), 260, 165; ^1H NMR ($CDCl_3$) δ 0.61 (3 H, s, angular Me), 9.99 (1 H, s, CHO); IR ($CHCl_3$) 2950, 1710 cm^{-1}. For the semicarbazone: mp 160–161 °C; MS, *m/e* 335 (M^+), 276; UV max (95% EtOH) 232 nm. Anal. Calcd. for $C_{20}H_{37}ON_3$: C, 71.59; H, 11.12; N, 12.53. Found: C, 71.83; H, 11.13; N, 12.27.

In a similar manner, **4a** (320 mg, 0.77 mmol) was treated with BF_3–etherate to yield **17a** (145 mg, 68%).

Reaction of Endoperoxides 3a and 4a with $ZnCl_2$. A mixture of **4a** (100 mg, 0.24 mmol) and $ZnCl_2$ (10 mg, 7.3×10^{-2} mmol) in xylene (2 mL) was heated at 100 °C for 5 min. The mixture was directly chromatographed on silica gel (5 g). Elution with ethyl acetate–hexane (35:65) gave aldehyde **17a** (57 mg, 85%).

In a similar manner, **3a** (24 mg, 5.8×10^{-2} mmol) was treated with $ZnCl_2$ to give **17a** (13 mg, 81%).

Isomerization of Aldehyde 17a to 17b. A solution of **17a** (10 mg) in ethanol (500 μL) was added to a solution of sodium ethoxide (prepared from 20 mg of Na) in ethanol (1 mL) at 0 °C, and the mixture was stirred at that temperature for 10 min. Ice chips were added, and the mixture was extracted with chloroform. The extract was washed with water, dried over Na_2SO_4, and evaporated. The residue was purified on TLC (silica gel, ethyl acetate–hexane 1:9) to give **17b**: 9 mg (90%); MS *m/e* 278 (M^+), 249; ^1H NMR ($CDCl_3$) δ 0.70 (3 H, s, angular Me), 9.53 (1 H, d, J = 3 Hz, CHO); IR ($CHCl_3$) 2950, 1720 cm^{-1}.

Reaction of Endoperoxides 3a and 4a with Methanolic Aqueous HCl. Concentrated hydrochloric acid (0.4 mL) was added to a solution of **3a** (58 mg) in methanol (4 mL) at 0 °C. The reaction mixture turned gradually to dark brown. After 2 h at 0 °C, ice chips were added, and the mixture was extracted with chloroform. The extract was washed with water, dried over Na_2SO_4, and evaporated. The residue was chromatographed on silica gel (5 g) with ethyl acetate–hexane (1:9) as the eluent to afford acetal **17c**: 17 mg (38%); MS, *m/e* 324 (M^+), 323, 293, 292, 278, 261; ^1H NMR ($CDCl_3$) δ 0.67 (3 H, s, angular Me), 3.38 (3 H, s, MeO), 3.40 (3 H, s, MeO), 4.06 (1 H, d, acetal proton); IR ($CHCl_3$) 2940 cm^{-1}.

In a similar manner, **4a** (74 mg) was treated with methanolic HCl to give acetal **17c** (20 mg, 35%).

Hydrolysis of Acetal 17c. To a solution of **17c** (17 mg) in acetone (2 mL) was added 18% aqueous hydrochloric acid (0.4 mL) at 0 °C, and the mixture was stirred at that temperature for 45 min. After dilution with water, the acetone was evaporated, and the aqueous residue was extracted with chloroform. The extract was washed with brine, dried over Na_2SO_4, and evaporated.

The residue was chromatographed on silica gel (3 g) to give **17b** (18 mg, quantitative).

Reaction of Endoperoxide 3a with Cobalt-Tetraphenylporphine. To a solution of CoTPP (3 mg, 4.5×10^{-3} mmol) in CH_2Cl_2 (1 mL) was added a solution of **3a** (20 mg, 4.8×10^{-2} mmol) in CH_2Cl_2 (1 mL) at −20 °C, and the mixture was stirred at −20 to −10 °C for 5 h. Evaporation of the solvent and chromatography of the residue on silica gel (5 g) with ethyl acetate-hexane (80:20) as the eluent afforded **13a** (15 mg, 75%).

Reaction of Endoperoxides 3a and 4a with Tetrakis(triphenylphosphine)palladium. A solution of **3a** (35 mg, 8.4×10^{-2} mmol) and $Pd(Ph_3P)_4$ (10 mg, 8.7×10^{-3} mmol) in benzene (1 mL) was refluxed for 15 min. The dark red reaction mixture was directly chromatographed on silica gel to afford **15a** (16 mg, 47%) (ethyl acetate–hexane, 20:80) and **13a** (5.5 mg, 16%) (ethyl acetate–hexane, 70:30).

In a similar manner, **4a** (50 mg) was treated with $Pd(Ph_3P)_4$ to give **15a** (25 mg, 52%) and **14a** (8 mg, 16%).

(6*R*)-9,10-Secocholesta-5(10),7-diene-3β,6,19-triol (9). Reduction of Endoperoxide 3a with $LiAlH_4$. A solution of **3a** (118 mg, 0.28 mmol) in dry ether (5 mL) was added to a suspension of $LiAlH_4$ (22 mg, 0.58 mmol) in ether (2 mL) at 0 °C. After 1 h at room temperature, the reaction was quenched with wet Na_2SO_4, and the mixture was filtered and washed with ethyl acetate–methanol (4:1). The combined filtrate and washings were evaporated, and the residue was chromatographed on Sephdex LH-20 (10 g) with hexane–chloroform (35:65) as the eluent to afford triol **9**: 83 mg (70%); MS, *m/e* 418 (M^+), 400, 382, 287, 269, 152, 134; ^1H NMR ($CDCl_3$) δ 0.50 (3 H, s, H-18), 3.88 (1 H, m, H-3), 4.05 (1 H, d, *J* = 12 Hz, H-19), 4.25 (1 H, d, *J* = 12 Hz, H-19), 5.14 (1 H, d, *J* = 8 Hz, H-6 or H-7), 5.34 (1 H, d, *J* = 8 Hz, H-7 or H-6); IR ($CHCl_3$) 3610, 3410, 2960 cm^{-1}.

(6*S*)-9,10-Secocholesta-5(10),7-diene-3β,6,19-triol (10). Reduction of Endoperoxide 4a with $LiAlH_4$. Reduction of **4a** (45 mg) with $LiAlH_4$ was followed the procedure described above to give triol **10**: 23 mg (51%); MS *m/e* 418 (M^+), 400, 287, 269, 153, 152, 135, 134; ^1H NMR ($CDCl_3$) δ 0.57 (3 H, s, H-18), 3.77 (1 H, d, *J* = 12 Hz, H-19), 4.10 (1 H, m, H-3), 4.47 (1 H, d, *J* = 12 Hz, H-19), 5.10 (1 H, d, *J* = 8 Hz, H-6 or H-7), 5.52 (1 H, d, *J* = 8 Hz, H-7 or H-6); IR ($CHCl_3$) 3620, 3410, 2955 cm^{-1}.

Registry No. **1a**, 67-97-0; **1b**, 50-14-6; **2a**, 22350-41-0; **2b**, 51744-66-2; **3a**, 73047-69-5; **3b**, 70779-98-5; **3c**, 70779-97-4; **4a**, 73047-65-1; **4b**, 70779-99-6; **4c**, 70801-88-6; **5a**, 86728-02-1; **5b**, 86728-03-2; **6a**, 86728-04-3; **6b**, 86728-05-4; **7a**, 86728-06-5; **8a**, 86728-07-6; **9a**, 86832-43-1; **10a**, 74532-19-7; **13a** C(19)-(*R*), 86728-08-7; **13a** C(19)-(*S*), 86832-09-8; **13b** C(19)-(*R*), 86832-44-2; **13b** C(19)-(*S*), 86832-45-3; **14a**, 86782-90-3; **14b** C(19)-(*R*), 86832-46-4; **14b** C(19)-(*S*), 86832-47-5; **15a**, 74546-09-1; **15b**, 86728-10-1; **16b**, 86728-11-2; **17a**, 86728-12-3; **17a** semicarbazone, 86728-13-4; **17b**, 86728-14-5; **17c**, 86728-15-6.

Stereoselective Synthesis of (5*E*)- and (5*Z*)-Vitamin D_3 19-Alkanoic Acids via Vitamin D_3–Sulfur Dioxide Adducts

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(5*E*)- and (5*Z*)-vitamin D_3 19-alkanoic acids **7** and **8** have been synthesized by a new method starting with vitamin D_3. In this synthesis, sulfur dioxide was utilized innovatively to protect the *s*-cis diene part of vitamin D and at the same time to activate the terminal position (C-19) of the diene group for an electrophilic substitution reaction. The two C-6 epimers of the vitamin D_3–sulfur dioxide adducts **2** and **3** were isolated in pure form, and the structure was determined unambiguously on the basis of X-ray analysis. The reaction of pure adducts **2b** and **3b** with *tert*-butyl ω-iodoalkanoate **4** proceeded with complete regio- and stereoselectivity to afford 19-alkanoic acid derivatives **5** and **6** in which the substituent at C-19 is located trans to that at C-6. Thermolytic desulfonylation of the 19-substituted adducts **5** and **6** in the presence of $NaHCO_3$ afforded (5*E*)-vitamin D_3 19-alkanoic acid derivatives **7** with high selectivity (ca. 93%), contrary to orbital symmetry rules. The (5*E*)-vitamin D derivatives **7** were converted to the corresponding (5*Z*)-vitamin D derivatives **8** in high selectivity (ca. 95%) by photosensitized isomerization.

Extensive studies on the metabolism of vitamin D_3 have lead to the discovery of more than 20 metabolites.[1] For clinical studies of the production of the biologically important metabolites, such as 1α,25-dihydroxyvitamin D_3, 24(*R*),25-dihydroxyvitamin D_3, etc., establishment of a sensitive, convenient, and selective analytical method has been needed. Radioimmunoassay has been highly successful for the measurement of steroid hormones. For use as an immunogen, a vitamin D molecule must be converted to a derivative appropriate for combining with a protein. Recently, we have developed a new regioselective method of alkylating vitamin D at the 6- and 19-positions via its sulfur dioxide adducts **2** and **3**.[2] In this method sulfur dioxide is used to protect the *s*-cis diene part of vitamin D, as well as to activate the terminal position of the diene group for electrophilic substitution reaction under basic conditions. We planned to apply the alkylation method to the synthesis of vitamin D_3 19-alkanoic acid derivatives **7** and **8**. The compounds **8** and **7** as components of a hapten are suitable derivatives for inducing antibodies for the radioimmunoassay of vitamin D and its 1α-hydroxylated derivatives, respectively. Because the biologically essential hydroxyl group remains intact[3] in **7** and

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